

## (12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
15 April 2004 (15.04.2004)

PCT

(10) International Publication Number  
**WO 2004/031155 A1**

(51) International Patent Classification<sup>7</sup>: **C07D 223/24**,  
C07F 15/00, A61K 31/55, A61P 25/08

(21) International Application Number:  
PCT/EP2003/011034

(22) International Filing Date: 6 October 2003 (06.10.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
0223224.7 7 October 2002 (07.10.2002) GB

(71) Applicant (for all designated States except AT, US): **NOVARTIS AG** [CH/CH]; Lichtstrasse 35, CH-4056 Basel (CH).

(71) Applicant (for AT only): **NOVARTIS PHARMA GMBH** [AT/AT]; Brunner Strasse 59, A-1230 Vienna (AT).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **MATHES, Christian** [DE/DE]; Spitzwegstrasse 4, 79618 Rheinfelden

(DE). **SEDELMEIER, Gottfried** [DE/DE]; Erlenweg 11, 79227 Schallstadt (DE). **BLATTER, Fritz** [CH/CH]; Oerinstrasse 67, CH-4153 Reinach (CH). **PFEFFER, Sabine** [DE/DE]; Beethovenstrasse 16, 79576 Weil (DE). **GRIMLER, Dominique** [FR/FR]; 14, rue des Bûcherons, F-68560 Hirsingue (FR).

(74) Agents: **GRUBB, Philipp** et al.; Novartis AG, Corporate Intellectual Property, CH-4002 Basel (CH).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SE, SG, SK, SY, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW.

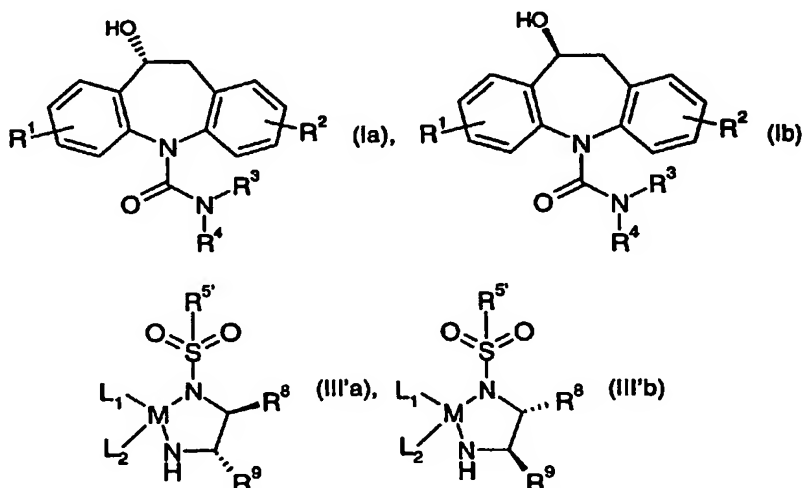
(84) Designated States (regional): Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR).

Published:

— with international search report

[Continued on next page]

(54) Title: **ENANTIOSELECTIVE PROCESS FOR THE PREPARATION OF BOTH ENANTIOMERS OF 10,11-DIHYDRO-10-HYDROXY-5H-DIBENZ [b,f]AZEPINE-5-CARBOXAMIDE AND NEW CRYSTAL FORMS THEREOF**



(57) Abstract: The invention relates to a novel process for the manufacture of substituted enantiopure 10hydroxy--dihydrodibenz[b,f]azepines (Ia), (Ib) wherein each of R<sup>1</sup> and R<sup>2</sup>, independently, are hydrogen, halogen, amino or nitro; and each of R<sup>3</sup> and R<sup>4</sup>, independently, are hydrogen or C<sub>1</sub>-C<sub>6</sub>alkyl; by transfer hydrogenation of 10-oxo-dihydrodibenz[b,f]azepines; and to novel catalysts of formula (III'a) and (III'b) wherein M is Ru, Rh, Ir, Fe, Co or Ni; L<sub>1</sub> is hydrogen; L<sub>2</sub> represents an aryl or aryl-aliphatic residue; and the further radicals have the meanings as defined herein; and to new crystal forms of both enantiomers of 10,11-dihydro-10 hydroxy-5Hdibenz[b,f]azepine-5-carboxamide, obtainable by the new processes, their usage in the production of pharmaceutical preparations, new pharmaceutical preparations comprising these new crystal forms and/or the use of these new crystal forms in the treatment of disorders such as epilepsy, or in the production of pharmaceutical formulations which are suitable for this treatment.



— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*